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LOGINID:SSSPTA1626GMS

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TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	DEC 18	CA/CAPLUS pre-1967 chemical substance index entries enhanced with preparation role
NEWS	4	DEC 18	CA/CAPLUS patent kind codes updated
NEWS	5	DEC 18	MARPAT to CA/CAPLUS accession number crossover limit increased to 50,000
NEWS	6	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS	7	DEC 27	CA/CAPLUS enhanced with more pre-1907 records
NEWS	8	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	9	JAN 16	CA/CAPLUS Company Name Thesaurus enhanced and reloaded
NEWS	10	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	11	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	12	JAN 22	CA/CAPLUS updated with revised CAS roles
NEWS	13	JAN 22	CA/CAPLUS enhanced with patent applications from India
NEWS	14	JAN 29	PHAR reloaded with new search and display fields
NEWS	15	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS	16	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS	17	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS	18	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS	19	FEB 26	MEDLINE reloaded with enhancements
NEWS	20	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS	21	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS	22	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS	23	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS	24	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS	25	MAR 16	CASREACT coverage extended
NEWS	26	MAR 20	MARPAT now updated daily
NEWS	27	MAR 22	LWPI reloaded
NEWS	28	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS	29	MAR 30	INPADOCDB will replace INPADOC on STN
NEWS	30	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS EXPRESS			NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS LOGIN			Welcome Banner and News Items
NEWS IPC8			For general information regarding STN implementation of IPC 8
NEWS X25			X.25 communication option no longer available

10521799.trn

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 07:16:33 ON 15 APR 2007

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 07:16:45 ON 15 APR 2007

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 APR 2007 HIGHEST RN 930268-90-9

DICTIONARY FILE UPDATES: 13 APR 2007 HIGHEST RN 930268-90-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

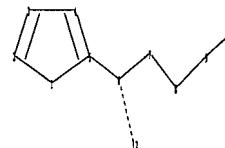
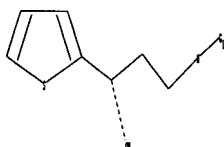
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10521799.str



```

chain nodes :
6 7 8 9 11 12
ring nodes :
1 2 3 4 5
chain bonds :
5-6 6-7 6-12 7-8 8-9 9-11
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
6-12 8-9 9-11
exact bonds :
1-2 1-5 2-3 3-4 4-5 5-6 6-7 7-8
isolated ring systems :
containing 1 :

```

G1:H,Ak

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS  
11:CLASS 12:CLASS

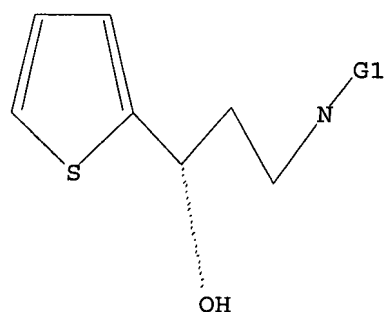
L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

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G1 H, Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 07:19:12 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 453 TO ITERATE

100.0% PROCESSED 453 ITERATIONS

15 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 7784 TO 10336

PROJECTED ANSWERS: 68 TO 532

L2 15 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 07:19:18 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 9242 TO ITERATE

100.0% PROCESSED 9242 ITERATIONS

SEARCH TIME: 00.00.01

328 ANSWERS

L3 328 SEA SSS FUL L1

=> FIL HCAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

173.90

174.11

FILE 'HCAPLUS' ENTERED AT 07:19:36 ON 15 APR 2007

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of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 15 Apr 2007 VOL 146 ISS 17  
FILE LAST UPDATED: 13 Apr 2007 (20070413/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 188 L3

=> s l4 and process

2409591 PROCESS

1638936 PROCESSES

3596091 PROCESS

(PROCESS OR PROCESSES)

L5 38 L4 AND PROCESS

=> s l5 and enantiomer

23897 ENANTIOMER

27436 ENANTIOMERS

39311 ENANTIOMER

(ENANTIOMER OR ENANTIOMERS)

L6 4 L5 AND ENANTIOMER

=> s l5 and enantiomer-enriched

23897 ENANTIOMER

27436 ENANTIOMERS

39311 ENANTIOMER

(ENANTIOMER OR ENANTIOMERS)

128305 ENRICHED

1 ENRICHEDS

128306 ENRICHED

(ENRICHED OR ENRICHEDS)

54 ENANTIOMER-ENRICHED

(ENANTIOMER(W) ENRICHED)

L7 0 L5 AND ENANTIOMER-ENRICHED

=> s l5 and catalyst

759789 CATALYST

757482 CATALYSTS

970541 CATALYST

(CATALYST OR CATALYSTS)

L8 15 L5 AND CATALYST

=> s l8 and bidentate

23787 BIDENTATE

128 BIDENTATES

23865 BIDENTATE

(BIDENTATE OR BIDENTATES)

L9 3 L8 AND BIDENTATE

=> s l8 and bidentate phosphorus

23787 BIDENTATE

128 BIDENTATES

23865 BIDENTATE

(BIDENTATE OR BIDENTATES)

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313451 PHOSPHORUS  
1 PHOSPHORUSES  
2 PHOSPHORI  
8 PHOSPHORIS  
313460 PHOSPHORUS  
(PHOSPHORUS OR PHOSPHORUSES OR PHOSPHORI OR PHOSPHORIS)

111 BIDENTATE PHOSPHORUS  
(BIDENTATE (W) PHOSPHORUS)  
L10 0 L8 AND BIDENTATE PHOSPHORUS

=> s l8 and enantiomer-enriched  
23897 ENANTIOMER  
27436 ENANTIOMERS  
39311 ENANTIOMER  
(ENANTIOMER OR ENANTIOMERS)  
128305 ENRICHED  
1 ENRICHEDS  
128306 ENRICHED  
(ENRICHED OR ENRICHEDS)  
54 ENANTIOMER-ENRICHED  
(ENANTIOMER (W) ENRICHED)  
L11 0 L8 AND ENANTIOMER-ENRICHED

=> s l8 and enantiomer  
23897 ENANTIOMER  
27436 ENANTIOMERS  
39311 ENANTIOMER  
(ENANTIOMER OR ENANTIOMERS)  
L12 3 L8 AND ENANTIOMER

=> d his

(FILE 'HOME' ENTERED AT 07:16:33 ON 15 APR 2007)

FILE 'REGISTRY' ENTERED AT 07:16:45 ON 15 APR 2007

L1 STRUCTURE UPLOADED  
L2 15 S L1  
L3 328 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 07:19:36 ON 15 APR 2007

L4 188 S L3  
L5 38 S L4 AND PROCESS  
L6 4 S L5 AND ENANTIOMER  
L7 0 S L5 AND ENANTIOMER-ENRICHED  
L8 15 S L5 AND CATALYST  
L9 3 S L8 AND BIDENTATE  
L10 0 S L8 AND BIDENTATE PHOSPHORUS  
L11 0 S L8 AND ENANTIOMER-ENRICHED  
L12 3 S L8 AND ENANTIOMER

=> d l6 ibib abs hitstr tot

L6 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:101154 HCAPLUS

DOCUMENT NUMBER: 140:163699

TITLE: Process for the preparation of  
3-hydroxy-(2-thienyl)propanamines by catalytic  
enantioselective hydrogenation of the corresponding  
ketones

INVENTOR(S): Hems, William; Rossen, Kai; Reichert, Dietmar;

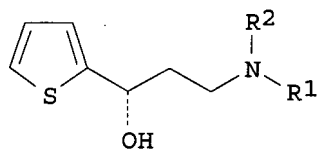
04/15/2007

Page 6

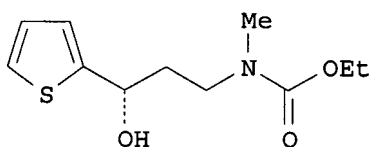
Koehler, Klaus; Almena Perea, Juan Jose  
 PATENT ASSIGNEE(S): Degussa A.-G., Germany  
 SOURCE: PCT Int. Appl., 27 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011452	A1	20040205	WO 2003-EP7927	20030721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10233724	A1	20040205	DE 2002-10233724	20020724
DE 10258098	A1	20040701	DE 2002-10258098	20021211
CA 2493228	A1	20040205	CA 2003-2493228	20030721
AU 2003258532	A1	20040216	AU 2003-258532	20030721
EP 1523479	A1	20050420	EP 2003-771063	20030721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1671685	A	20050921	CN 2003-817590	20030721
JP 2006502996	T	20060126	JP 2004-523756	20030721
US 2005272930	A1	20051208	US 2005-521799	20050121
IN 2005KN00259	A	20070105	IN 2005-KN259	20050224
PRIORITY APPLN. INFO.:			DE 2002-10233724	A 20020724
			DE 2002-10258098	A 20021211
			WO 2003-EP7927	W 20030721

OTHER SOURCE(S): CASREACT 140:163699; MARPAT 140:163699  
 GI



I



II

AB Title compds. I [wherein R1 and R2 = independently H, (cyclo)alkyl, acyl, alkoxy carbonyl, (hetero)aryl, (hetero)aralkyl, alkylcycloalkyl, alkyl(hetero)aryl; or NR1R2 = (un)substituted heterocyclyl], intermediates for the synthesis of enantiomer-pure bioactive substances, were prepared by catalytic enantioselective hydrogenation of the corresponding  $\alpha$ -heteroaryl ketones. Inter alia Ru catalysts with chiral diamine and chiral biphosphine ligands were used. For example, 3-[N-ethoxycarbonyl-N-methylamino]-1-(2-thienyl)-1-propanone was introduced to a Buchi stirred autoclave, which was then evacuated. A mixture of (R)-TolBINAP-RuCl<sub>2</sub>-(1R,2R)-diphenylethylenediamine and KOBu-t in iPrOH was added. Flushing with H<sub>2</sub>, pressurizing to 10 bar, and heating to 40° for 2 h provided II in >96% yield with an enantiomeric excess

of 80.1%. The content of cyclic carbamate byproduct increased significantly after standing for a fairly long time.

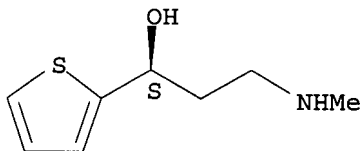
IT 116539-55-0P

RL: IMF (Industrial manufacture); PREP (Preparation)  
(preparation of 3-hydroxy-(2-thienyl)propanamines by catalytic enantioselective hydrogenation of corresponding ketones)

RN 116539-55-0 HCAPLUS

CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



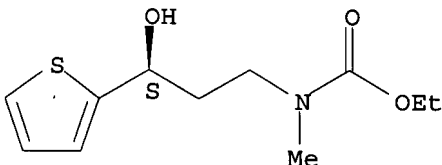
IT 586968-34-5P, (S)-3-[N-(Ethoxycarbonyl)-N-methylamino]-1-(2-thienyl)-1-propanol

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 3-hydroxy-(2-thienyl)propanamines by catalytic enantioselective hydrogenation of corresponding ketones)

RN 586968-34-5 HCAPLUS

CN Carbamic acid, [(3S)-3-hydroxy-3-(2-thienyl)propyl]methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:931354 HCAPLUS

DOCUMENT NUMBER: 139:395802

TITLE: Preparation of propanolamine derivatives, process for preparation of 3-N-methylamino-1-(2-thienyl)-1-propanols, and process for preparation of propanolamine derivatives

INVENTOR(S): Inoue, Yoshiki; Mori, Hiroyuki; Nogami, Hiroyuki; Saitou, Takayuki; Ogura, Kuniyoshi

PATENT ASSIGNEE(S): Mitsubishi Rayon Co., Ltd., Japan

SOURCE: PCT Int. Appl., 98 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

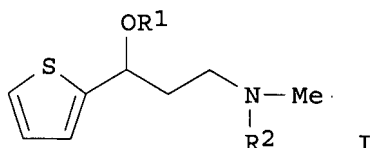
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

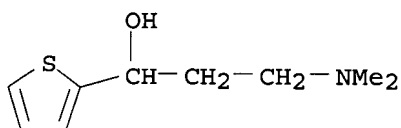
PATENT INFORMATION:



PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097632	A1	20031127	WO 2003-JP6225	20030519
W: CN, JP, US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
EP 1506965	A1	20050216	EP 2003-752916	20030519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006167278	A1	20060727	US 2005-513790	20050527
PRIORITY APPLN. INFO.:			JP 2002-145394	A 20020520
			JP 2001-256621	A 20010827
			WO 2003-JP6225	W 20030519
OTHER SOURCE(S):		MARPAT 139:395802		
GI				

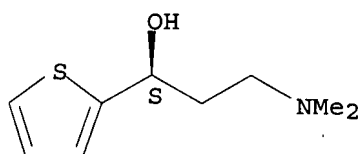


- AB A process is provided, by which 3-N-methylamino-1-(2-thienyl)-1-propanols represented by the general formula (I) (wherein R1 is hydrogen, C1-8 acyl, substituted or unsubstituted C1-8 alkyloxycarbonyl, or substituted or unsubstituted phenyloxycarbonyl; and R2 is hydrogen, C1-8 alkyl, substituted or unsubstituted benzyl, C1-8 acyl, substituted or unsubstituted C1-8 alkyloxycarbonyl, or substituted or unsubstituted phenyloxycarbonyl, with the proviso that a case wherein R1 is hydrogen and R2 is Me or hydrogen is excepted) can be easily prepared in the form of a racemate or an optically active substance of S- or R-configuration at a low cost and in a high yield. The compds. I are useful as intermediates for drugs and agrochems., e.g. (S)-enantiomer for duloxetine (antidepressant). Thus, 36.9 g N-benzylmethylamine (0.30 mmol) was dissolved in 40 mL ethanol, treated with 30.0 g 37% aqueous HCl (0.30 mmol) to convert it to the hydrochloride salt, treated with 30 g 2-acetylthiophene, 10.8 g paraformaldehyde, 20 mL ethanol, and 1.2 g 37% aqueous HCl (0.01 mmol), heated at 80° under reflux for 4 h, cooled to room temperature, and filtered, followed by washing the crystals with ethanol and drying under reduced pressure to give 57.7 g 3-(N-benzylmethylamino)-1-(2-thienyl)-1-propanone (II) as the HCl salt. A 0.5 M KOH/2-propanol (40 µL), 2.1 mg (R,R)-1,2-diphenylethylenediamine, 873 mg II, and 3 mL 2-propanol were added to a Schlenk reaction tube, degassed and purged with Ar, treated with 9.6 mg RuCl<sub>2</sub>((R)-BINAP)(DMF)<sub>n</sub>, repeatedly degassed and purged with Ar, dissolved completely, transferred to a glass autoclave, pressurized with H<sub>2</sub>, and stirred at 28° for 6 h to give (S)-3-(N-benzylmethylamino)-1-(2-thienyl)-1-propanol (96% ee).
- IT 13636-02-7, 3-(Dimethylamino)-1-(2-thienyl)-1-propanol  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of (methylamino)thienylpropanols)
- RN 13636-02-7 HCAPLUS
- CN 2-Thiophenemethanol, α-[2-(dimethylamino)ethyl]- (CA INDEX NAME)

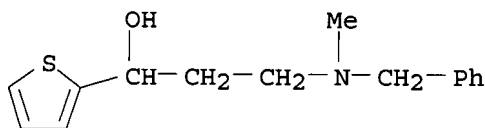


IT 132335-44-5P 138760-50-6P 625853-14-7P  
 625853-20-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of (methylamino)thienylpropanols)  
 RN 132335-44-5 HCAPLUS  
 CN 2-Thiophenemethanol,  $\alpha$ -[2-(dimethylamino)ethyl]-, ( $\alpha$ S)- (CA  
 INDEX NAME)

Absolute stereochemistry. Rotation (-).

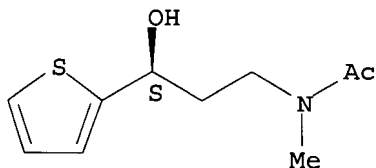


RN 138760-50-6 HCAPLUS  
 CN 2-Thiophenemethanol,  $\alpha$ -[2-[methyl(phenylmethyl)amino]ethyl]- (9CI)  
 (CA INDEX NAME)



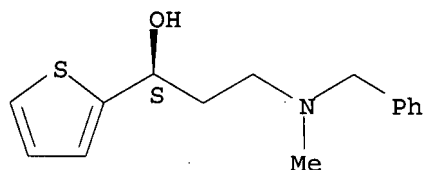
RN 625853-14-7 HCAPLUS  
 CN Acetamide, N-[(3S)-3-hydroxy-3-(2-thienyl)propyl]-N-methyl- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



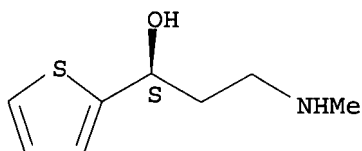
RN 625853-20-5 HCAPLUS  
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 ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

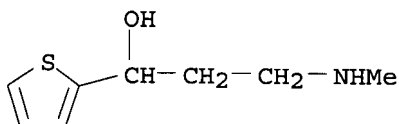


IT 116539-55-0P 116539-56-1P 625853-17-0P  
 625853-28-3P 625853-29-4P 625853-30-7P  
 625853-31-8P 625853-32-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of (methylamino)thienylpropanols)  
 RN 116539-55-0 HCAPLUS  
 CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ S)- (CA  
 INDEX NAME)

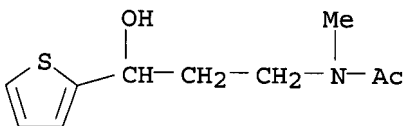
Absolute stereochemistry. Rotation (-).



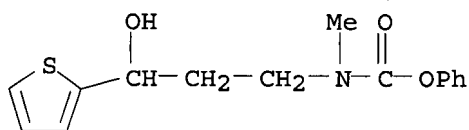
RN 116539-56-1 HCAPLUS  
 CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]- (CA INDEX NAME)



RN 625853-17-0 HCAPLUS  
 CN Acetamide, N-[3-hydroxy-3-(2-thienyl)propyl]-N-methyl- (9CI) (CA INDEX  
 NAME)

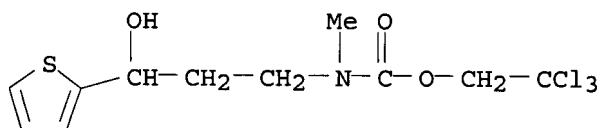


RN 625853-28-3 HCAPLUS  
 CN Carbamic acid, [3-hydroxy-3-(2-thienyl)propyl]methyl-, phenyl ester (9CI)  
 (CA INDEX NAME)



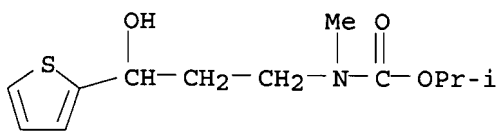
RN 625853-29-4 HCAPLUS

CN Carbamic acid, [3-hydroxy-3-(2-thienyl)propyl]methyl-,  
2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)



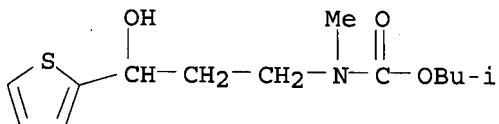
RN 625853-30-7 HCAPLUS

CN Carbamic acid, [3-hydroxy-3-(2-thienyl)propyl]methyl-, 1-methylethyl ester  
(9CI) (CA INDEX NAME)



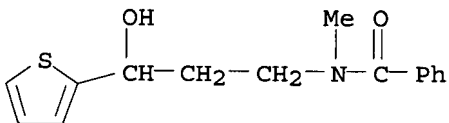
RN 625853-31-8 HCAPLUS

CN Carbamic acid, [3-hydroxy-3-(2-thienyl)propyl]methyl-, 2-methylpropyl  
ester (9CI) (CA INDEX NAME)



RN 625853-32-9 HCAPLUS

CN Benzamide, N-[3-hydroxy-3-(2-thienyl)propyl]-N-methyl- (9CI) (CA INDEX  
NAME)



REFERENCE COUNT:

22

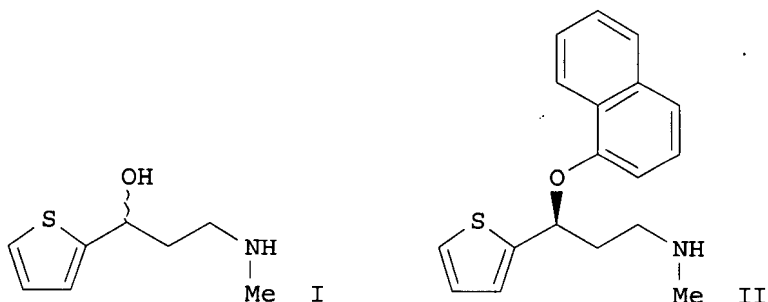
THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:591163 HCAPLUS  
 DOCUMENT NUMBER: 139:149519  
 TITLE: Process for preparing (S)-3-methylamino-1-(2-thienyl)-1-propanol, an intermediate useful for the asymmetric synthesis of duloxetine, via optical resolution  
 INVENTOR(S): Borghese, Alfio  
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
 SOURCE: PCT Int. Appl., 12 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062219	A1	20030731	WO 2003-US18	20030113
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1478641	A1	20041124	EP 2003-707289	20030113
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
US 2004249170	A1	20041209	US 2004-500829	20040707
PRIORITY APPLN. INFO.:			US 2002-351622P	P 20020124
			WO 2003-US18	W 20030113

GI



AB The invention provides an optical resolution process for the synthesis of (S)-3-methylamino-1-(2-thienyl)-1-propanol [(S)-I], a key intermediate in the synthesis of duloxetine (II) and its hydrochloride. The process comprises 3 distinct steps. The first step involves resolution of racemic I using either 2,3,4,6-di-O-isopropylidene-2-keto-L-gulonic acid (III) or (S)-(-)-2-pyrrolidone-5-carboxylic acid as the resolving agent, in a solvent which is preferably iso-PrOH, THF, acetone, or EtOAc, most preferably iso-PrOH. The second step involves racemization of a stereochem. enriched mixture, which may be the undesired isomer (R)-I,

and which may be carried out with HCl in iso-PrOH. The third step is a second order asym. induced crystallization of (S)-I, carried out by resolution of

racemic I using III as the resolving agent, in a solvent as described above. For instance, a solution of racemic I in iso-PrOH was treated with III, stirred, and filtered to give the diastereomeric salt (S)-I.III in 74% yield and 12% d.e. (diastereomeric excess). Re-suspension of the product salt in iso-PrOH followed by stirring at room temperature and filtration

(twice) increased the d.e. to 78% with losses in yield. In a demonstration of the racemization step, I.III with a d.e. of 75% was treated with 1N HCl for 2.5 h and concentrated in vacuo to give a solid showing a d.e. of 32%. In a demonstration of the 3rd step, racemic I and III in iso-PrOH were heated at 40° for 66 h and cooled and filtered to give crystalline (S)-I.III in 76% yield and 76% d.e. Mass balance anal. showed formation of the desired diastereomer at the expense of the unwanted one.

IT 569687-76-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (diastereomeric salt; process for preparation of a chiral duloxetine intermediate by optical resolution)

RN 569687-76-9 HCAPLUS

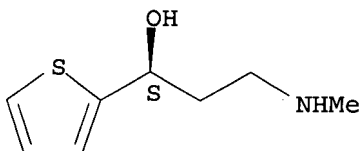
CN  $\alpha$ -L-xylo-2-Hexulofuranosonic acid, 2,3:4,6-bis-O-(1-methylethylidene)-, compd. with ( $\alpha$ S)- $\alpha$ -[2-(methylamino)ethyl]-2-thiophenemethanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 116539-55-0

CMF C8 H13 N O S

Absolute stereochemistry. Rotation (-).

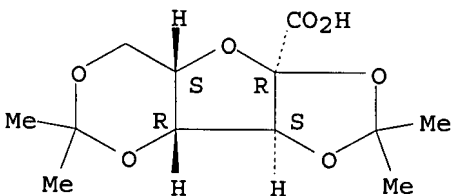


CM 2

CRN 18467-77-1

CMF C12 H18 O7

Absolute stereochemistry. Rotation (-).



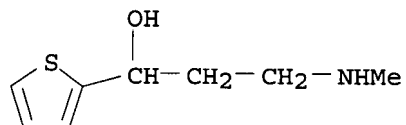
IT 116539-56-1, 3-Methylamino-1-(2-thienyl)-1-propanol

RL: RCT (Reactant); RACT (Reactant or reagent)

(racemic starting material; process for preparation of a chiral duloxetine intermediate by optical resolution)

RN 116539-56-1 HCAPLUS

CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]- (CA INDEX NAME)



IT 116539-57-2P, (R)-3-Methylamino-1-(2-thienyl)-1-propanol

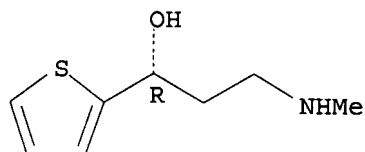
RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(racemization as undesired enantiomer; process for preparation of a chiral duloxetine intermediate by optical resolution)

RN 116539-57-2 HCAPLUS

CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 116539-55-0P, (S)-3-Methylamino-1-(2-thienyl)-1-propanol

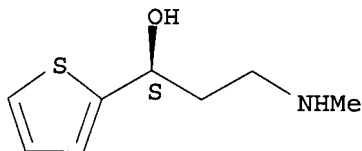
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(target intermediate; process for preparation of a chiral duloxetine intermediate by optical resolution)

RN 116539-55-0 HCAPLUS

CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:405867 HCAPLUS

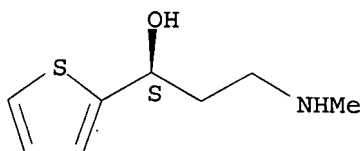
DOCUMENT NUMBER: 139:245838

TITLE: Chemoenzymatic synthesis of duloxetine and its enantiomer: lipase-catalyzed resolution of 3-hydroxy-3-(2-thienyl) propanenitrile

10521799.trn

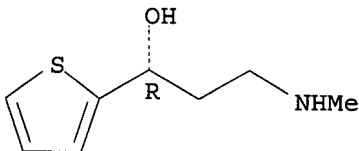
AUTHOR(S): Kamal, Ahmed; Khanna, G. B. Ramesh; Ramu, R.;  
Krishnaji, T.  
CORPORATE SOURCE: Division of Organic Chemistry, Biotransformation  
Laboratory, Indian Institute of Chemical Technology,  
Hyderabad, 500 007, India  
SOURCE: Tetrahedron Letters (2003), 44(25), 4783-4787  
CODEN: TELEAY; ISSN: 0040-4039  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 139:245838  
AB An efficient and facile chemoenzymic synthesis of duloxetine by  
lipase-mediated resolution of 3-hydroxy-3-(2-thienyl)propanenitrile has been  
achieved. This process also describes an enantioconvergent  
synthesis of duloxetine via a Mitsunobu reaction.  
IT 116539-55-0P 116539-57-2P 597581-29-8P  
597581-30-1P 597581-31-2P  
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); RCT  
(Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or  
reagent)  
(chemoenzymic synthesis of duloxetine and its enantiomers via  
lipase-catalyzed resolution of hydroxy(thienyl)propanenitrile and its use  
in enantioconvergent synthesis of duloxetine via Mitsunobu reaction)  
RN 116539-55-0 HCAPLUS  
CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ S)- (CA  
INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 116539-57-2 HCAPLUS  
CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ R)- (CA  
INDEX NAME)

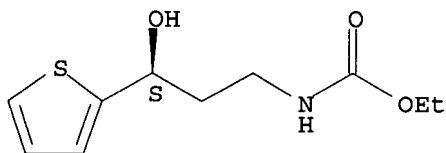
Absolute stereochemistry. Rotation (+).



RN 597581-29-8 HCAPLUS  
CN Carbamic acid, [(3S)-3-hydroxy-3-(2-thienyl)propyl]-, ethyl ester (9CI)  
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

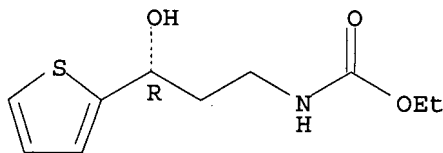




RN 597581-30-1 HCAPLUS

CN Carbamic acid, [(3R)-3-hydroxy-3-(2-thienyl)propyl]-, ethyl ester (9CI)  
(CA INDEX NAME)

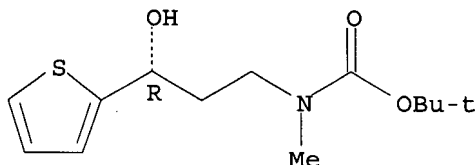
Absolute stereochemistry. Rotation (+).



RN 597581-31-2 HCAPLUS

CN Carbamic acid, [(3R)-3-hydroxy-3-(2-thienyl)propyl]methyl-,  
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=&gt; d 19 ibib abs hitstr tot

L9 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:181066 HCAPLUS

DOCUMENT NUMBER: 142:280046

TITLE: Process for the asymmetric hydrogenation of  
β-amino ketones using transition metal complexes  
of chiral bidentate phosphines as  
catalysts.

PATENT ASSIGNEE(S): Lonza AG, Switz.

SOURCE: Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

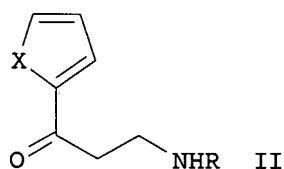
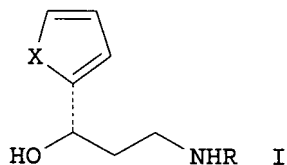
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

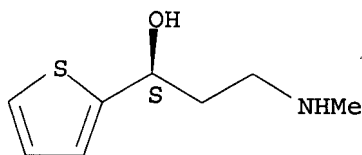
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 1510517 A1 20050302 EP 2003-77734 20030901  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 AU 2004268057 A1 20050310 AU 2004-268057 20040831  
 WO 2005021527 A2 20050310 WO 2004-EP9690 20040831  
 WO 2005021527 A3 20050714  
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,  
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,  
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
 SN, TD, TG  
 EP 1664014 A2 20060607 EP 2004-764655 20040831  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK  
 CN 1842523 A 20061004 CN 2004-80024598 20040831  
 JP 2007504192 T 20070301 JP 2006-525092 20040831  
 NO 2006000763 A 20060317 NO 2006-763 20060217  
 US 2006252945 A1 20061109 US 2006-569824 20060228  
 PRIORITY APPLN. INFO.: EP 2003-77734 A 20030901  
 WO 2004-EP9690 W 20040831  
 OTHER SOURCE(S): CASREACT 142:280046; MARPAT 142:280046  
 GI



AB A process for the preparation of enantiomerically enriched or enantiomerically pure  $\beta$ -amino alcs. [I; X = S, O; R = (substituted) alkyl, cycloalkyl, aryl, aralkyl] comprises asym. hydrogenation of ketones (II; variables as above) using transition metal complexes of chiral bidentate phosphines as catalysts. Thus, 3-methylamino-1-(thien-2-yl)propan-1-one hydrochloride (preparation given), NaOMe, (S,S)-Me-DuPhos, and [Rh(COD)<sub>2</sub>]BF<sub>4</sub> were autoclaved together in MeOH at 30-34° and 30 bar H<sub>2</sub> for 5 h to give 67% (S)-3-methylamino-1-(2-thienyl)-1-propanol in >99% enantiomeric excess.  
 IT 116539-55-0P, (S)-3-Methylamino-1-(2-thienyl)-1-propanol  
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (asym. hydrogenation of aminoketones using transition metal complexes of chiral bidentate phosphines as catalysts)  
 RN 116539-55-0 HCAPLUS  
 CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:101154 HCAPLUS

DOCUMENT NUMBER: 140:163699

TITLE: Process for the preparation of 3-hydroxy-(2-thienyl)propanamines by catalytic enantioselective hydrogenation of the corresponding ketones

INVENTOR(S): Hems, William; Rossen, Kai; Reichert, Dietmar; Koehler, Klaus; Almendra Perea, Juan Jose

PATENT ASSIGNEE(S): Degussa A.-G., Germany

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

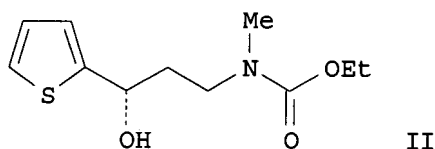
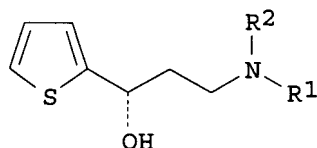
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011452	A1	20040205	WO 2003-EP7927	20030721
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10233724	A1	20040205	DE 2002-10233724	20020724
DE 10258098	A1	20040701	DE 2002-10258098	20021211
CA 2493228	A1	20040205	CA 2003-2493228	20030721
AU 2003258532	A1	20040216	AU 2003-258532	20030721
EP 1523479	A1	20050420	EP 2003-771063	20030721
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1671685	A	20050921	CN 2003-817590	20030721
JP 2006502996	T	20060126	JP 2004-523756	20030721
US 2005272930	A1	20051208	US 2005-521799	20050121
IN 2005KN00259	A	20070105	IN 2005-KN259	20050224
PRIORITY APPLN. INFO.:			DE 2002-10233724	A 20020724
			DE 2002-10258098	A 20021211
			WO 2003-EP7927	W 20030721

OTHER SOURCE(S): CASREACT 140:163699; MARPAT 140:163699

GI



AB Title compds. I [wherein R1 and R2 = independently H, (cyclo)alkyl, acyl, alkoxy carbonyl, (hetero)aryl, (hetero)aralkyl, alkylcycloalkyl, alkyl(hetero)aryl; or NR1R2 = (un)substituted heterocyclyl], intermediates for the synthesis of enantiomer-pure bioactive substances, were prepared by catalytic enantioselective hydrogenation of the corresponding  $\alpha$ -heteroaryl ketones. Inter alia Ru catalysts with chiral diamine and chiral biphosphine ligands were used. For example, 3-[N-ethoxycarbonyl-N-methylamino]-1-(2-thienyl)-1-propanone was introduced to a Buchi stirred autoclave, which was then evacuated. A mixture of (R)-TolBINAP-RuCl<sub>2</sub>-(1R,2R)-diphenylethylenediamine and KOBu-t in iPrOH was added. Flushing with H<sub>2</sub>, pressurizing to 10 bar, and heating to 40° for 2 h provided II in >96% yield with an enantiomeric excess of 80.1%. The content of cyclic carbamate byproduct increased significantly after standing for a fairly long time.

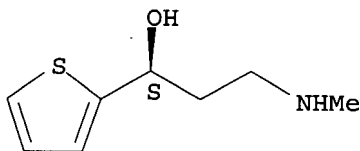
IT 116539-55-0P

RL: IMF (Industrial manufacture); PREP (Preparation)  
(preparation of 3-hydroxy-(2-thienyl)propanamines by catalytic enantioselective hydrogenation of corresponding ketones)

RN 116539-55-0 HCAPLUS

CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 586968-34-5P, (S)-3-[N-(Ethoxycarbonyl)-N-methylamino]-1-(2-thienyl)-1-propanol

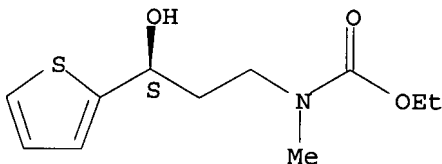
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 3-hydroxy-(2-thienyl)propanamines by catalytic enantioselective hydrogenation of corresponding ketones)

RN 586968-34-5 HCAPLUS

CN Carbamic acid, [(3S)-3-hydroxy-3-(2-thienyl)propyl]methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:757296 HCAPLUS

DOCUMENT NUMBER: 139:276809

TITLE: Process for preparing nonracemic chiral alcohols

INVENTOR(S): Tucker, Charles E.; Jiang, Qiongzong

PATENT ASSIGNEE(S): DSM N.V., Neth.

SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S.Ser.No. 57,826.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003181319	A1	<del>20030925</del>	US 2002-158560	20020521
US 2003144521	A1	20030731	US 2002-57826	20020124
US 6743921	B2	20040601		
<del>WO 2003061826</del>	A1	<del>20030731</del>	WO 2002-NL827	20021213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2002-57826 A2 20020124  
US 2002-158560 A 20020521

OTHER SOURCE(S): MARPAT 139:276809

AB The present invention provides a catalyst system and a process for the preparation of a nonracemic chiral alc. by hydrogenation of a ketone using the catalyst system, wherein the catalyst system comprises ruthenium, a nonracemic chiral diphosphine ligand, a bidentate amine ligand, and an organic base selected from alkylamidines, alkylguanidines, aminophosphazenes, and proazaphosphatranes. Thus, in a dry nitrogen-filled glovebox, a 20-mL glass reaction vial was charged with 5 mL 250  $\mu$ L (1.25  $\mu$ mol) [RuCl<sub>2</sub>(R,R,R,R-BICP)(DMF)<sub>n</sub>] (preparation given) in isopropanol, 5 mL isopropanol, and 125  $\mu$ L 0.1 M (12.5  $\mu$ mol) ethylenediamine in isopropanol. After stirring for several minutes, 73  $\mu$ L (625  $\mu$ mol) acetophenone was added, followed by 0.50 mL 0.1 M (50  $\mu$ mol) tetramethyl-2-tert-butylguanidine in isopropanol. The glass reaction vial containing the resulting mixture was sealed in an autoclave and then removed from the glovebox. The gas phase in the autoclave was replaced by hydrogen at 18 bar and the reaction mixture was stirred at room temperature

for 6

h under 17-18 bar hydrogen to give, after silica gel chromatog., (S)-1-phenylethanol (77% e.e.).

IT 132335-44-5P, (S)-3-(Dimethylamino)-1-(2-thienyl)-1-propanol

RL: SPN (Synthetic preparation); PREP (Preparation)

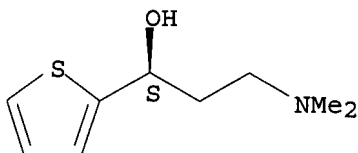
(preparation of nonracemic chiral alcs. by stereoselective hydrogenation of ketone using catalyst system, comprising ruthenium complex,

nonracemic chiral diphosphine ligand, bidentate amine ligand,  
and organic base)

RN 132335-44-5 HCAPLUS

CN 2-Thiophenemethanol,  $\alpha$ -[2-(dimethylamino)ethyl]-, ( $\alpha$ S)- (CA  
INDEX NAME)

Absolute stereochemistry. Rotation (-).



=> d l12 ibib abs hitstr tot

L12 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:101154 HCAPLUS

DOCUMENT NUMBER: 140:163699

TITLE: Process for the preparation of  
3-hydroxy-(2-thienyl)propanamines by catalytic  
enantioselective hydrogenation of the corresponding  
ketones

INVENTOR(S): Hems, William; Rossen, Kai; Reichert, Dietmar;  
Koehler, Klaus; Almendra Perea, Juan Jose

PATENT ASSIGNEE(S): Degussa A.-G., Germany

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011452	A1	20040205	WO 2003-EP7927	20030721
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10233724	A1	20040205	DE 2002-10233724	20020724
DE 10258098	A1	20040701	DE 2002-10258098	20021211
CA 2493228	A1	20040205	CA 2003-2493228	20030721
AU 2003258532	A1	20040216	AU 2003-258532	20030721
EP 1523479	A1	20050420	EP 2003-771063	20030721
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1671685	A	20050921	CN 2003-817590	20030721
JP 2006502996	T	20060126	JP 2004-523756	20030721
US 2005272930	A1	20051208	US 2005-521799	20050121

IN 2005KN00259  
PRIORITY APPLN. INFO.:

A 20070105

IN 2005-KN259

20050224

DE 2002-10233724

A 20020724

DE 2002-10258098

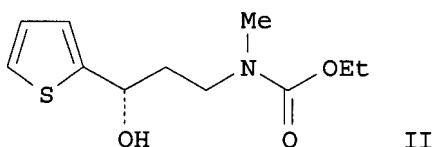
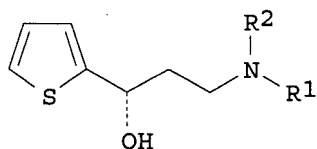
A 20021211

WO 2003-EP7927

W 20030721

OTHER SOURCE(S):  
GI

CASREACT 140:163699; MARPAT 140:163699



AB Title compds. I [wherein R1 and R2 = independently H, (cyclo)alkyl, acyl, alkoxy carbonyl, (hetero)aryl, (hetero)aralkyl, alkylcycloalkyl, alkyl(hetero)aryl; or NR1R2 = (un)substituted heterocyclyl], intermediates for the synthesis of enantiomer-pure bioactive substances, were prepared by catalytic enantioselective hydrogenation of the corresponding  $\alpha$ -heteroaryl ketones. Inter alia Ru catalysts with chiral diamine and chiral biphosphine ligands were used. For example, 3-[N-ethoxycarbonyl-N-methylamino]-1-(2-thienyl)-1-propanone was introduced to a Buchi stirred autoclave, which was then evacuated. A mixture of (R)-TolBINAP-RuCl<sub>2</sub>-(1R,2R)-diphenylethylenediamine and KOBu-t in iPrOH was added. Flushing with H<sub>2</sub>, pressurizing to 10 bar, and heating to 40° for 2 h provided II in >96% yield with an enantiomeric excess of 80.1%. The content of cyclic carbamate byproduct increased significantly after standing for a fairly long time.

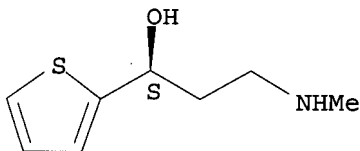
IT 116539-55-0P

RL: IMF (Industrial manufacture); PREP (Preparation)  
(preparation of 3-hydroxy-(2-thienyl)propanamines by catalytic enantioselective hydrogenation of corresponding ketones)

RN 116539-55-0 HCAPLUS

CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



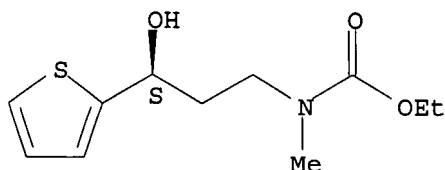
IT 586968-34-5P, (S)-3-[N-(Ethoxycarbonyl)-N-methylamino]-1-(2-thienyl)-1-propanol

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 3-hydroxy-(2-thienyl)propanamines by catalytic enantioselective hydrogenation of corresponding ketones)

RN 586968-34-5 HCAPLUS

CN Carbamic acid, [(3S)-3-hydroxy-3-(2-thienyl)propyl]methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:931354 HCAPLUS

DOCUMENT NUMBER: 139:395802

TITLE: Preparation of propanolamine derivatives, process for preparation of 3-N-methylamino-1-(2-thienyl)-1-propanols, and process for preparation of propanolamine derivatives

INVENTOR(S): Inoue, Yoshiki; Mori, Hiroyuki; Nogami, Hiroyuki; Saitou, Takayuki; Ogura, Kuniyoshi

PATENT ASSIGNEE(S): Mitsubishi Rayon Co., Ltd., Japan

SOURCE: PCT Int. Appl., 98 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

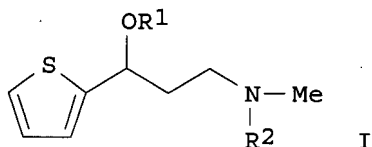
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097632	A1	20031127	WO 2003-JP6225	20030519
W: CN, JP, US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
EP 1506965	A1	20050216	EP 2003-752916	20030519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006167278	A1	20060727	US 2005-513790	20050527
PRIORITY APPLN. INFO.:			JP 2002-145394	A 20020520
			JP 2001-256621	A 20010827
			WO 2003-JP6225	W 20030519

OTHER SOURCE(S): MARPAT 139:395802  
GI



AB A process is provided, by which 3-N-methylamino-1-(2-thienyl)-1-propanols represented by the general formula (I) (wherein R1 is hydrogen, C1-8 acyl, substituted or unsubstituted C1-8 alkyloxycarbonyl, or substituted or unsubstituted phenyloxycarbonyl; and R2 is hydrogen, C1-8



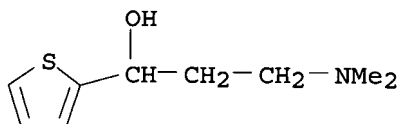
alkyl, substituted or unsubstituted benzyl, C1-8 acyl, substituted or unsubstituted C1-8 alkyloxycarbonyl, or substituted or unsubstituted phenyloxycarbonyl, with the proviso that a case wherein R1 is hydrogen and R2 is Me or hydrogen is excepted) can be easily prepared in the form of a racemate or an optically active substance of S- or R-configuration at a low cost and in a high yield. The compds. I are useful as intermediates for drugs and agrochems., e.g. (S)-enantiomer for duloxetine (antidepressant). Thus, 36.9 g N-benzylmethylamine (0.30 mmol) was dissolved in 40 mL ethanol, treated with 30.0 g 37% aqueous HCl (0.30 mmol) to convert it to the hydrochloride salt, treated with 30 g 2-acetylthiophene, 10.8 g paraformaldehyde, 20 mL ethanol, and 1.2 g 37% aqueous HCl (0.01 mmol), heated at 80° under reflux for 4 h, cooled to room temperature, and filtered, followed by washing the crystals with ethanol and drying under reduced pressure to give 57.7 g 3-(N-benzylmethylamino)-1-(2-thienyl)-1-propanone (II) as the HCl salt. A 0.5 M KOH/2-propanol (40  $\mu$ L), 2.1 mg (R,R)-1,2-diphenylethylenediamine, 873 mg II, and 3 mL 2-propanol were added to a Schlenk reaction tube, degassed and purged with Ar, treated with 9.6 mg RuCl<sub>2</sub>((R)-BINAP)(DMF)<sub>n</sub>, repeatedly degassed and purged with Ar, dissolved completely, transferred to a glass autoclave, pressurized with H<sub>2</sub>, and stirred at 28° for 6 h to give (S)-3-(N-benzylmethylamino)-1-(2-thienyl)-1-propanol (96% ee).

IT 13636-02-7, 3-(Dimethylamino)-1-(2-thienyl)-1-propanol

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of (methylamino)thienylpropanols)

RN 13636-02-7 HCAPLUS

CN 2-Thiophenemethanol,  $\alpha$ -[2-(dimethylamino)ethyl]- (CA INDEX NAME)



IT 132335-44-5P 138760-50-6P 625853-14-7P

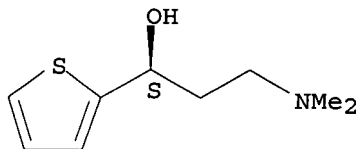
625853-20-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of (methylamino)thienylpropanols)

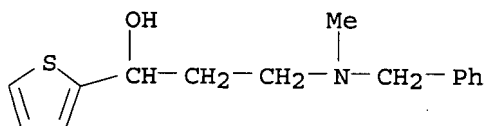
RN 132335-44-5 HCAPLUS

CN 2-Thiophenemethanol,  $\alpha$ -[2-(dimethylamino)ethyl]-, ( $\alpha$ S)- (CA INDEX NAME)



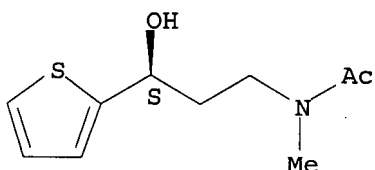
RN 138760-50-6 HCAPLUS

CN 2-Thiophenemethanol,  $\alpha$ -[2-[methyl(phenylmethyl)amino]ethyl]- (9CI)  
(CA INDEX NAME)



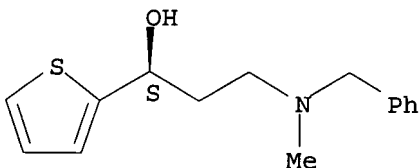
RN 625853-14-7 HCAPLUS  
 CN Acetamide, N-[(3S)-3-hydroxy-3-(2-thienyl)propyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



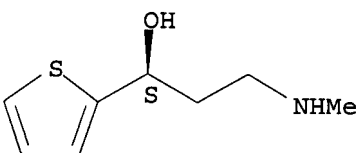
RN 625853-20-5 HCAPLUS  
 CN 2-Thiophenemethanol,  $\alpha$ -[2-[methyl(phenylmethyl)amino]ethyl]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

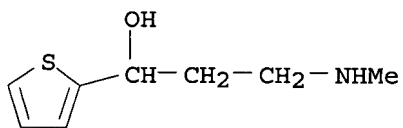


IT 116539-55-0P 116539-56-1P 625853-17-0P  
 625853-28-3P 625853-29-4P 625853-30-7P  
 625853-31-8P 625853-32-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of (methylamino)thienylpropanols)  
 RN 116539-55-0 HCAPLUS  
 CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ S)- (CA INDEX NAME)

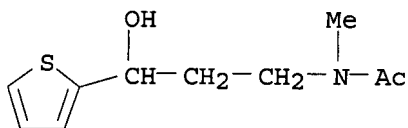
Absolute stereochemistry. Rotation (-).



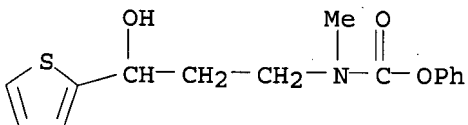
RN 116539-56-1 HCAPLUS  
 CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]- (CA INDEX NAME)



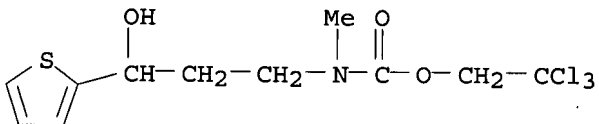
RN 625853-17-0 HCAPLUS  
 CN Acetamide, N-[3-hydroxy-3-(2-thienyl)propyl]-N-methyl- (9CI) (CA INDEX NAME)



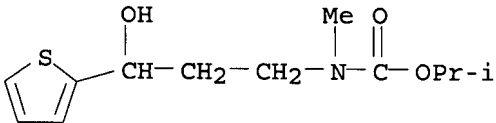
RN 625853-28-3 HCAPLUS  
 CN Carbamic acid, [3-hydroxy-3-(2-thienyl)propyl]methyl-, phenyl ester (9CI) (CA INDEX NAME)



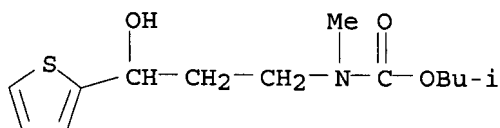
RN 625853-29-4 HCAPLUS  
 CN Carbamic acid, [3-hydroxy-3-(2-thienyl)propyl]methyl-, 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)



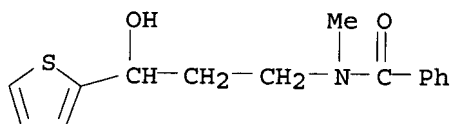
RN 625853-30-7 HCAPLUS  
 CN Carbamic acid, [3-hydroxy-3-(2-thienyl)propyl]methyl-, 1-methylethyl ester (9CI) (CA INDEX NAME)



RN 625853-31-8 HCAPLUS  
 CN Carbamic acid, [3-hydroxy-3-(2-thienyl)propyl]methyl-, 2-methylpropyl ester (9CI) (CA INDEX NAME)



RN 625853-32-9 HCAPLUS  
 CN Benzamide, N-[3-hydroxy-3-(2-thienyl)propyl]-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:405867 HCAPLUS

DOCUMENT NUMBER: 139:245838

TITLE: Chemoenzymatic synthesis of duloxetine and its enantiomer: lipase-catalyzed resolution of 3-hydroxy-3-(2-thienyl) propanenitrile

AUTHOR(S): Kamal, Ahmed; Khanna, G. B. Ramesh; Ramu, R.; Krishnaji, T.

CORPORATE SOURCE: Division of Organic Chemistry, Biotransformation Laboratory, Indian Institute of Chemical Technology, Hyderabad, 500 007, India

SOURCE: Tetrahedron Letters (2003), 44 (25), 4783-4787

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:245838

AB An efficient and facile chemoenzymic synthesis of duloxetine by lipase-mediated resolution of 3-hydroxy-3-(2-thienyl)propanenitrile has been achieved. This process also describes an enantioconvergent synthesis of duloxetine via a Mitsunobu reaction.

IT 116539-55-0P 116539-57-2P 597581-29-8P  
 597581-30-1P 597581-31-2P

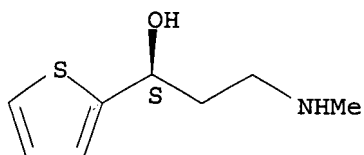
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(chemoenzymic synthesis of duloxetine and its enantiomers via lipase-catalyzed resolution of hydroxy(thienyl)propanenitrile and its use in enantioconvergent synthesis of duloxetine via Mitsunobu reaction)

RN 116539-55-0 HCAPLUS

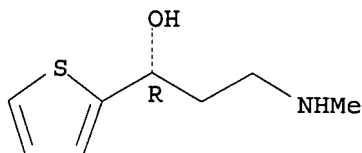
CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



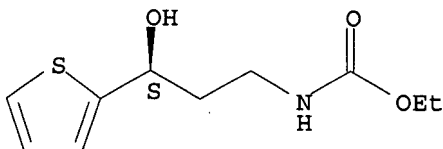
RN 116539-57-2 HCAPLUS  
 CN 2-Thiophenemethanol,  $\alpha$ -[2-(methylamino)ethyl]-, ( $\alpha$ R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



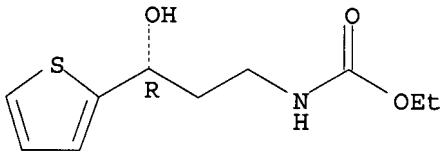
RN 597581-29-8 HCAPLUS  
 CN Carbamic acid, [(3S)-3-hydroxy-3-(2-thienyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



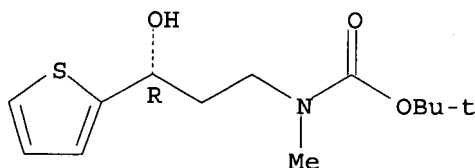
RN 597581-30-1 HCAPLUS  
 CN Carbamic acid, [(3R)-3-hydroxy-3-(2-thienyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 597581-31-2 HCAPLUS  
 CN Carbamic acid, [(3R)-3-hydroxy-3-(2-thienyl)propyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L8 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2006:1251751 HCAPLUS  
 DOCUMENT NUMBER: 146:27718  
 TITLE: Etherification and resolution and demethylation process for the preparation of duloxetine and its acid-addition salts  
 INVENTOR(S): Satyanarayana, Chava; Ramanjaneyulu, Gorantla Seeta; Ramdas, Chavakula; Rao, Konudula Babu  
 PATENT ASSIGNEE(S): Matrix Laboratories Ltd, India  
 SOURCE: PCT Int. Appl., 18pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006126213	A1	20061130	WO 2006-IN174	20060523
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: IN 2005-CH623 A 20050524

OTHER SOURCE(S): CASREACT 146:27718

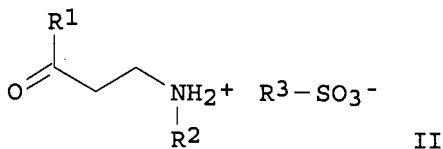
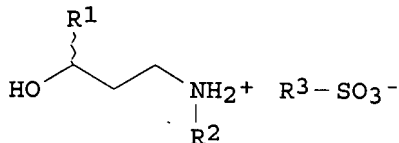
AB A process for preparing duloxetine, or its acid addition salts (e.g., the hydrochloride), comprises: (A) the etherification of (S)-(-)-N,N-dimethyl-3-(2-thienyl)-3-hydroxypropanamine with 1-fluoronaphthalene, followed by demethylation, or etherification of N,N-dimethyl-3-(2-thienyl)-3-hydroxypropanamine with 1-fluoronaphthalene followed by resolution and demethylation; and (B) if desired, the neutralization of duloxetine free base into an acid-addition salt.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2006:866581 HCAPLUS

DOCUMENT NUMBER: 145:271387  
 TITLE: Process for the preparation of enantiomerically pure 1-substituted-3-amino alcohols using methyl ketones, primary amines, formaldehydes and sulfonic acids  
 INVENTOR(S): Brieden, Walter; Clausen, Martin; McGarrity, John; Mettler, Hanspeter; Michel, Dominique  
 PATENT ASSIGNEE(S): Lonza A.-G., Switz.  
 SOURCE: PCT Int. Appl., 38pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006087166	A1	20060824	WO 2006-EP1334	20060214
W:	AE, AG, AL, AM, AT, AU, <del>AZ</del> , BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, <del>DE</del> , DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
EP 1693371	A1	20060823	EP 2005-3657	20050221
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU			
PRIORITY APPLN. INFO.:			EP 2005-3657	A 20050221
OTHER SOURCE(S):			CASREACT 145:271387; MARPAT 145:271387	
GI				



AB Provided is a process for the preparation of N-monosubstituted  $\beta$ -aminoalc. sulfonates of formula I. Compds. of formula I wherein R<sup>1</sup> is (un)substituted C<sub>6</sub>-20 aryl or (un)substituted C<sub>4</sub>-12 heteroaryl; R<sup>2</sup> is C<sub>1</sub>-4-alkyl or (un)substituted C<sub>6</sub>-20 aryl; R<sup>3</sup> is selected from the group consisting of C<sub>1</sub>-18 alkyl, C<sub>6</sub>-20 cycloalkyl, C<sub>6</sub>-20 aryl and C<sub>7</sub>-20 aralkyl residues, and the process for preparing compds. of formula I are claimed. The process comprising the steps of a) reacting a Me ketone, a primary amine, formaldehyde and a sulfonic acid, at a pressure above 1.5 bar, optionally in a organic solvent, said organic solvent optionally containing water, to afford N-monosubstituted  $\beta$ -amino ketone sulfonates of formula II, wherein R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are as defined above, and b) asym. hydrogenating said sulfonates in the presence of a base and a catalyst, comprising a transition metal and a diphosphine ligand,

in a polar solvent, optionally in the presence of water.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

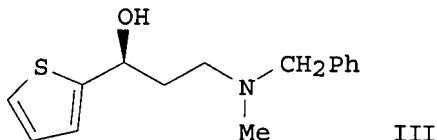
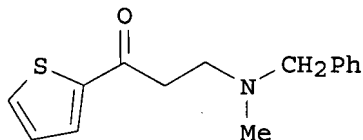
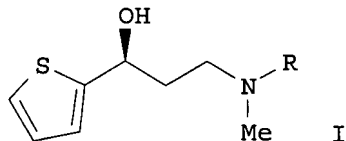
L8 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2005:985346 HCAPLUS  
 DOCUMENT NUMBER: 143:286275  
 TITLE: Process for the preparation of  
 N-alkyl-N-methyl-3-hydroxy-3-(2-thienyl)-propylamines  
 INVENTOR(S): Schiffers, Robert; Kreye, Paul; Baumgarten, Wolfgang;  
 Collet, Rosemarie  
 PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany  
 SOURCE: U.S. Pat. Appl. Publ., 7 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005197503	A1	20050908	US 2005-60510	20050216
DE 102004032828	A1	20060223	DE 2004-102004032828	20040706
CA 2556994	A1	20050915	CA 2005-2556994	20050226
WO 2005085192	A1	20050915	WO 2005-EP2047	20050226

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2004-5272 A 20040305  
 DE 2004-102004032828A 20040706  
 WO 2005-EP2047 W 20050226

OTHER SOURCE(S): CASREACT 143:286275; MARPAT 143:286275  
 GI



AB An improved process for preparing chiral N-substituted  
 N-methyl-3-hydroxy-3-(2-thienyl)-propylamines of formula I [R = C1-6 alkyl]



group optionally substituted by Ph, or an acid addition salt thereof] on an industrial scale is reported. An asym. hydrogenation using a catalyst system consisting of rhodium and (2R, 4R)-4-(dicyclohexylphosphino)-2-(diphenyl-phosphino-methyl)-N-methyl-aminocarbonyl-pyrrolidine is the key step. Thus II·HCl is hydrogenated at 40° C and 50 bar hydrogen pressure for about 20 h in the presence of bis-(1,5-cyclooctadiene)dirhodium(I)dichloride and (2R,4R)-4-(dicyclohexylphosphino)-2-(diphenyl-phosphino-methyl)-N-methyl-aminocarbonyl-pyrrolidine to provide III in 98% enantiomeric purity after workup.

L8 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:181066 HCAPLUS

DOCUMENT NUMBER: 142:280046

TITLE: Process for the asymmetric hydrogenation of  $\beta$ -amino ketones using transition metal complexes of chiral bidentate phosphines as catalysts.

PATENT ASSIGNEE(S): Lonza AG, Switz.

SOURCE: Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

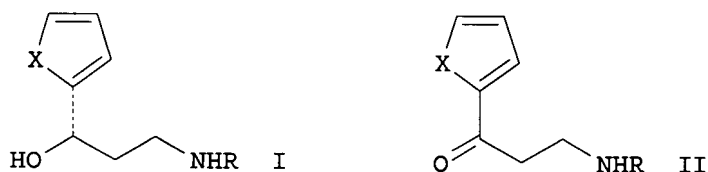
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1510517	A1	20050302	EP 2003-77734	20030901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004268057	A1	20050310	AU 2004-268057	20040831
WO 2005021527	A2	20050310	WO 2004-EP9690	20040831
WO 2005021527	A3	20050714		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1664014	A2	20060607	EP 2004-764655	20040831
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1842523	A	20061004	CN 2004-80024598	20040831
JP 2007504192	T	20070301	JP 2006-525092	20040831
NO 2006000763	A	20060317	NO 2006-763	20060217
US 2006252945	A1	20061109	US 2006-569824	20060228
PRIORITY APPLN. INFO.:			EP 2003-77734	A 20030901
			WO 2004-EP9690	W 20040831
OTHER SOURCE(S):			CASREACT 142:280046; MARPAT 142:280046	
GI				



AB A process for the preparation of enantiomerically enriched or enantiomerically pure  $\beta$ -amino alcs. [I; X = S, O; R = (substituted) alkyl, cycloalkyl, aryl, aralkyl] comprises asym. hydrogenation of ketones (II; variables as above) using transition metal complexes of chiral bidentate phosphines as catalysts. Thus, 3-methylamino-1-(thien-2-yl)propan-1-one hydrochloride (preparation given), NaOMe, (S,S)-Me-DuPhos, and [Rh(COD)2]BF4 were autoclaved together in MeOH at 30-34° and 30 bar H2 for 5 h to give 67% (S)-3-methylamino-1-(2-thienyl)-1-propanol in >99% enantiomeric excess.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:1037091 HCAPLUS

DOCUMENT NUMBER: 142:23180

TITLE: Process for producing optically active N-monoalkyl-3-hydroxy-3-arylpropylamine compound and intermediate

INVENTOR(S): Iwakura, Kazunori; Higashii, Takayuki; Bando, Seiji

PATENT ASSIGNEE(S): Sumitomo Seika Chemicals Co. Ltd., Japan

SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103990	A1	20041202	WO 2004-JP6602	20040511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

JP 2004346008 A 20041209 JP 2003-144742 20030522

PRIORITY APPLN. INFO.: JP 2003-144742 A 20030522

OTHER SOURCE(S): CASREACT 142:23180; MARPAT 142:23180

AB There is provided a process for producing an optically active N-monoalkyl-3-oxo-3-arylpropylamine compound represented by the formula  $\text{ArC}^*\text{H}(\text{OH})\text{CH}_2\text{CH}_2\text{NHR}_1$  (wherein symbol \* indicates an asym. carbon atom; R1 represents optionally substituted C1-5 alkyl; Ar represents optionally substituted aryl or heteroaryl) characterized by asym. reducing a (Z)-protected-N-monoalkyl-3-oxo-3-arylpropenylamine compound represented by

the formula (Z)-ArCOCH:CHNR1R2 (wherein Ar and R1 are same as defined above; R2 represents an amino-protecting group) with an asym. catalyst to give an optically active compound represented by the formula ArC\*H(OH)CH2CH2NR1R2 (wherein the symbol \*, Ar, R1, and R2 are same as defined above) and successively eliminating the protective group (R2). Thus, 16.7 g (Z)-N-methyl-3-oxo-3-(2-thienyl)propenylamine was acylated by 16.4 g iso-Bu chlorocarbonate in the presence of 1.2 g 4-dimethylaminopyridine and 12.1 g Et3N in 200 mL tert-Bu Me ether at 50° for 28 h to give 22.0 g N-methyl-N-isobutoxycarbonyl-[(Z)-3-oxo-3-(2-thienyl)propenyl]amine (I). I (33.8 mg) was stirred in 2-propanol in the presence of potassium tert-butoxide and 2.3 mg [(S)-N-phenyl-2-azetidinecarboxamide]ruthenium(p-cymene) chloride (REG 543689-61-8) at 80° for 4 h to give 84% N-methyl-N-isobutoxycarbonyl-3-hydroxy-3-(2-thienyl)propylamine which (114.8 mg) was treated with a mixture of 0.2 g 30 weight% aqueous NaOH and 5 mL 2-propanol at 30° for 24 h to give N-methyl-3-hydroxy-3-(2-thienyl)propylamine (50% ee).

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:546493 HCAPLUS

DOCUMENT NUMBER: 141:106360

TITLE: A process of preparation of (+)-duloxetine

INVENTOR(S): Rao, Dharmaraj Ramachandra; Kankan, Rajendra Narayanrao; Wain, Christopher Paul

PATENT ASSIGNEE(S): Cipla Ltd, India

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

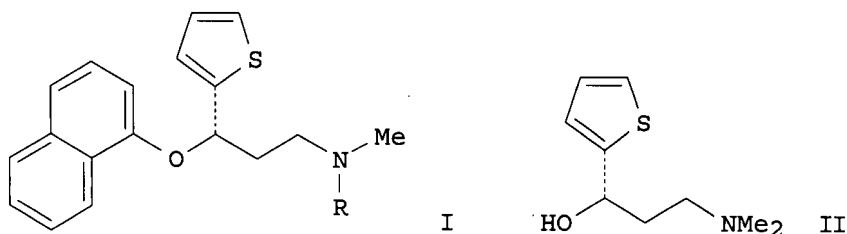
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056795	A1	20040708	WO 2003-GB5357	20031210
WO 2004056795	A8	20050811		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2510750	A1	20040708	CA 2003-2510750	20031210
AU 2003292396	A1	20040714	AU 2003-292396	20031210
BR 2003016902	A	20051025	BR 2003-16902	20031210
EP 1587801	A1	20051026	EP 2003-767973	20031210
EP 1587801	B1	20070131		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1747947	A	20060315	CN 2003-80109793	20031210
JP 2006514030	T	20060427	JP 2004-561607	20031210
EP 1690861	A2	20060816	EP 2006-75798	20031210
EP 1690861	A3	20060906		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK			

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AT 353081	T	20070215	AT 2003-767973	20031210
IN 2005MN00657	A	20050930	IN 2005-MN657	20050623
US 2006205956	A1	20060914	US 2006-539415	20060320
PRIORITY APPLN. INFO.:			GB 2002-29583	A 20021219
			EP 2003-767973	A3 20031210
			WO 2003-GB5357	W 20031210
OTHER SOURCE(S):		CASREACT 141:106360; MARPAT 141:106360		
GI				



AB The invention relates to a process for preparing (+)-duloxetine (I), or an acid addition salt thereof, which comprises (a) resolving racemic ( $\pm$ )-duloxetine with a chiral acid so as to obtain a salt of the chiral acid and (+)-duloxetine, substantially free of (-)-duloxetine; and (b) if desired, converting the salt prepared in step (a) to the free base or another acid addition salt as appropriate. The process for preparing (+)-duloxetine, or an acid addition salt thereof, can further comprise an O-alkylation intermediate process step which is carried out in the presence of a base and a phase transfer catalyst. For instance, (S)-duloxetine hydrochloride ( $I \cdot HCl$ ,  $R = H$ ) was prepared via etherification of alc. II by 1-fluoronaphthalene in the presence of 18-crown-6, and subsequent N-demethylation of the obtained oxalate salt of I ( $R = Me$ ) (example 4 and 5).

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:120843 HCAPLUS

DOCUMENT NUMBER: 140:181317

TITLE: Preparation of enantiomerically pure (S)-3-methylamino-1-(thien-2-yl)propan-1-ol from racemic 3-hydroxy-3-(thien-2-yl)propionitrile via kinetic resolution with an acylating agent and a lipase followed by treatment with methylamine and hydrogen in the presence of a catalyst.

INVENTOR(S): Stuermer, Rainer

PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013123	A1	20040212	WO 2003-EP8492	20030731
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,  
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,  
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 DE 10235206 A1 20040219 DE 2002-10235206 20020801  
 CA 2493451 A1 20040212 CA 2003-2493451 20030731  
 AU 2003251677 A1 20040223 AU 2003-251677 20030731  
 EP 1527065 A1 20050504 EP 2003-766383 20030731  
 EP 1527065 B1 20061122  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 CN 1671687 A 20050921 CN 2003-818510 20030731  
 JP 2006507234 T 20060302 JP 2004-525403 20030731  
 AT 346061 T 20061215 AT 2003-766383 20030731  
 US 2005245749 A1 20051103 US 2005-522888 20050624  
 PRIORITY APPLN. INFO.: DE 2002-10235206 A 20020801  
 WO 2003-EP8492 W 20030731

OTHER SOURCE(S): CASREACT 140:181317

AB A process for the preparation of enantiomerically pure  
 (S)-3-methylamino-1-(thien-2-yl)propan-1-ol (I) comprises treatment of of  
 a mixture of (R)- and (S)-3-hydroxy-3-thien-2-ylpropionitrile with an  
 acylating agent in the presence of a hydrolase to give a mixture of  
 unacylated (S)-3-hydroxy-3-thien-2-ylpropionitrile and acylated  
 (R)-nitrile and treatment of the former with hydrogen and methylamine in  
 the presence of a catalyst. Thus, 3-hydroxy-3-thien-2-  
 ylpropionitrile (preparation given) was shaken with lipase from Pseudomonas DSM  
 8246 and vinyl hexanoate in Me tert-Bu ether for 6 h at room temperature to  
 give  
 after flash chromatog. 48% (S)-3-hydroxy-3-thien-2-ylpropionitrile in  
 99.4% enantiomeric excess. The latter was autoclaved with MeNH<sub>2</sub> in MeOH  
 over Raney Ni under 50 bar H<sub>2</sub> at 65° for 24 h to give 79% I.

L8 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:101154 HCAPLUS

DOCUMENT NUMBER: 140:163699

TITLE: Process for the preparation of  
 3-hydroxy-(2-thienyl)propanamines by catalytic  
 enantioselective hydrogenation of the corresponding  
 ketones

INVENTOR(S): Hems, William; Rossen, Kai; Reichert, Dietmar;  
 Koehler, Klaus; Almendra Perea, Juan Jose

PATENT ASSIGNEE(S): Degussa A.-G., Germany

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

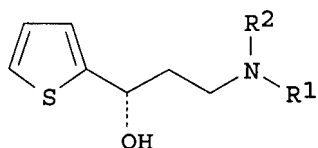
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

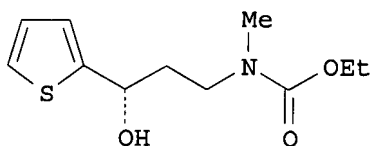
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011452	A1	20040205	WO 2003-EP7927	20030721
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,			

PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,  
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10233724	A1	20040205	DE 2002-10233724	20020724
DE 10258098	A1	20040701	DE 2002-10258098	20021211
CA 2493228	A1	20040205	CA 2003-2493228	20030721
AU 2003258532	A1	20040216	AU 2003-258532	20030721
EP 1523479	A1	20050420	EP 2003-771063	20030721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1671685	A	20050921	CN 2003-817590	20030721
JP 2006502996	T	20060126	JP 2004-523756	20030721
US 2005272930	A1	20051208	US 2005-521799	20050121
IN 2005KN00259	A	20070105	IN 2005-KN259	20050224
PRIORITY APPLN. INFO.:			DE 2002-10233724	A 20020724
			DE 2002-10258098	A 20021211
			WO 2003-EP7927	W 20030721
OTHER SOURCE(S):			CASREACT 140:163699; MARPAT 140:163699	
GI				



I



II

AB Title compds. I [wherein R1 and R2 = independently H, (cyclo)alkyl, acyl, alkoxy carbonyl, (hetero)aryl, (hetero)aralkyl, alkylcycloalkyl, alkyl(hetero)aryl; or NR1R2 = (un)substituted heterocyclyl], intermediates for the synthesis of enantiomer-pure bioactive substances, were prepared by catalytic enantioselective hydrogenation of the corresponding  $\alpha$ -heteroaryl ketones. Inter alia Ru catalysts with chiral diamine and chiral biphosphine ligands were used. For example, 3-[N-ethoxycarbonyl-N-methylamino]-1-(2-thienyl)-1-propanone was introduced to a Buchi stirred autoclave, which was then evacuated. A mixture of (R)-TolBINAP-RuCl<sub>2</sub>-(1R,2R)-diphenylethylenediamine and KOBu-t in iPrOH was added. Flushing with H<sub>2</sub>, pressurizing to 10 bar, and heating to 40° for 2 h provided II in >96% yield with an enantiomeric excess of 80.1%. The content of cyclic carbamate byproduct increased significantly after standing for a fairly long time.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:931354 HCAPLUS

DOCUMENT NUMBER: 139:395802

TITLE: Preparation of propanolamine derivatives, process for preparation of 3-N-methylamino-1-(2-thienyl)-1-propanols, and process for preparation of propanolamine derivatives

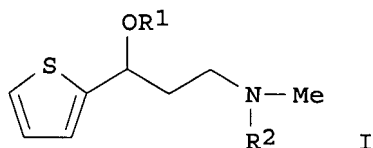
INVENTOR(S): Inoue, Yoshiki; Mori, Hiroyuki; Nogami, Hiroyuki; Saitou, Takayuki; Ogura, Kuniyoshi

PATENT ASSIGNEE(S): Mitsubishi Rayon Co., Ltd., Japan

SOURCE: PCT Int. Appl., 98 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097632	A1	20031127	WO 2003-JP6225	20030519
W: CN, JP, US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
EP 1506965	A1	20050216	EP 2003-752916	20030519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006167278	A1	20060727	US 2005-513790	20050527
PRIORITY APPLN. INFO.:			JP 2002-145394	A 20020520
			JP 2001-256621	A 20010827
			WO 2003-JP6225	W 20030519

OTHER SOURCE(S): MARPAT 139:395802  
 GI



AB A process is provided, by which 3-N-methylamino-1-(2-thienyl)-1-propanols represented by the general formula (I) (wherein R1 is hydrogen, C1-8 acyl, substituted or unsubstituted C1-8 alkyloxycarbonyl, or substituted or unsubstituted phenyloxycarbonyl; and R2 is hydrogen, C1-8 alkyl, substituted or unsubstituted benzyl, C1-8 acyl, substituted or unsubstituted C1-8 alkyloxycarbonyl, or substituted or unsubstituted phenyloxycarbonyl, with the proviso that a case wherein R1 is hydrogen and R2 is Me or hydrogen is excepted) can be easily prepared in the form of a racemate or an optically active substance of S- or R-configuration at a low cost and in a high yield. The compds. I are useful as intermediates for drugs and agrochems., e.g. (S)-enantiomer for duloxetine (antidepressant). Thus, 36.9 g N-benzylmethylamine (0.30 mmol) was dissolved in 40 mL ethanol, treated with 30.0 g 37% aqueous HCl (0.30 mmol) to convert it to the hydrochloride salt, treated with 30 g 2-acetylthiophene, 10.8 g paraformaldehyde, 20 mL ethanol, and 1.2 g 37% aqueous HCl (0.01 mmol), heated at 80° under reflux for 4 h, cooled to room temperature, and filtered, followed by washing the crystals with ethanol and drying under reduced pressure to give 57.7 g 3-(N-benzylmethylamino)-1-(2-thienyl)-1-propanone (II) as the HCl salt. A 0.5 M KOH/2-propanol (40 µL), 2.1 mg (R,R)-1,2-diphenylethylenediamine, 873 mg II, and 3 mL 2-propanol were added to a Schlenk reaction tube, degassed and purged with Ar, treated with 9.6 mg RuCl<sub>2</sub>((R)-BINAP)(DMF)<sub>n</sub>, repeatedly degassed and purged with Ar, dissolved completely, transferred to a glass autoclave, pressurized with H<sub>2</sub>, and stirred at 28° for 6 h to give (S)-3-(N-benzylmethylamino)-1-(2-thienyl)-1-propanol (96% ee).

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:757695 HCAPLUS

DOCUMENT NUMBER: 139:261165

TITLE: Process for preparation of

3-hydroxy-3-(2-thienyl)propionamide derivatives  
 INVENTOR(S): Takehara, Jun; Qu, Jingping; Kanno, Kazuaki; Kawabata, Hiroshi; Dekishima, Yasumasa; Ueda, Makoto; Endo, Kyoko; Murakami, Takeshi; Sasaki, Tomoko; Uehara, Hisatoshi; Matsumoto, Youichi; Suzuki, Shihomi

PATENT ASSIGNEE(S): Mitsubishi Chemical Corporation, Japan

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

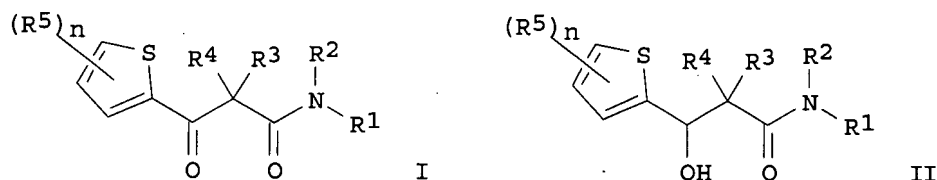
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078418	A1	20030925	WO 2003-JP3170	20030317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2003335732	A	20031128	JP 2002-141145	20020516
JP 2004067559	A	20040304	JP 2002-227401	20020805
JP 2004067560	A	20040304	JP 2002-227402	20020805
JP 2004067577	A	20040304	JP 2002-228495	20020806
JP 2003342275	A	20031203	JP 2002-317857	20021031
AU 2003221028	A1	20030929	AU 2003-221028	20030317
EP 1486493	A1	20041215	EP 2003-712723	20030317
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2004155756	A	20040603	JP 2003-102914	20030407
US 2005107621	A1	20050519	US 2004-944055	20040920
PRIORITY APPLN. INFO.:				
			JP 2002-76168	A 20020319
			JP 2002-129140	A 20020430
			JP 2002-141145	A 20020516
			JP 2002-227401	A 20020805
			JP 2002-227402	A 20020805
			JP 2002-228495	A 20020806
			JP 2002-267617	A 20020913
			JP 2002-317857	A 20021031
			WO 2003-JP3170	W 20030317

OTHER SOURCE(S): MARPAT 139:261165

GI





AB This invention pertains to a method for producing 3-oxo-3-(2-thienyl)propionamides with general formula of I [wherein R1 and R2 = independently H, alkyl, aryl, or aralkyl; R3 and R4 = independently H or alkyl; or R3 and R4 together form a ring with the nitrogen atom attached; R5 = halo, NO<sub>2</sub>, OH, (un)substituted alkyl, aryl, or alkoxy; n = 0-3] and a process for industrially producing optically active 3-amino-1-(2-thienyl)-1-propanol derivs. with general formula of II at low cost from the propionamides in high yields with high optical purity. The process comprises subjecting a β-ketocarbonyl compound having a thiophene ring to asym. reduction either in the presence of a catalyst comprising a compound of a Group 8 or 9 metal of the Periodic Table (e.g., ruthenium compound) and an asym. ligand (e.g., diphenylethylenediamine derivative) or using cells of a microorganism. Thus, 2-acetylthiophene was treated with NaH in THF, followed by the addition of di-Et carbonate to give 3-oxo-3-(2-thienyl)propionic acid Et ester (74%). The ester was treated with HCO<sub>2</sub>H in DMF in the presence of SS-TsDPEN and Et<sub>3</sub>N to provide (S)-3-hydroxy-3-(2-thienyl)propionic acid Et ester (94%) with 97.5% e.e. The chiral ester was treated with MeNH<sub>2</sub> in MeOH to afford (S)-3-hydroxy-N-methyl-3-(2-thienyl)propionamide (93%) with 99% e.e.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:757296 HCAPLUS

DOCUMENT NUMBER: 139:276809

TITLE: Process for preparing nonracemic chiral alcohols

INVENTOR(S): Tucker, Charles E.; Jiang, Qiongzong

PATENT ASSIGNEE(S): DSM N.V., Neth.

SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. Ser. No. 57,826.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003181319	A1	20030925	US 2002-158560	20020521
US 2003144521	A1	20030731	US 2002-57826	20020124
US 6743921	B2	20040601		
WO 2003061826	A1	20030731	WO 2002-NL827	20021213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-57826 A2 20020124  
 US 2002-158560 A 20020521

OTHER SOURCE(S): MARPAT 139:276809

AB The present invention provides a catalyst system and a process for the preparation of a nonracemic chiral alc. by hydrogenation of a ketone using the catalyst system, wherein the catalyst system comprises ruthenium, a nonracemic chiral diphosphine ligand, a bidentate amine ligand, and an organic base selected from alkylamidines, alkylguanidines, aminophosphazenes, and proazaphosphatranes. Thus, in a dry nitrogen-filled glovebox, a 20-mL glass reaction vial was charged with 5 mL 250  $\mu$ L (1.25  $\mu$ mol) [RuCl<sub>2</sub>(R,R,R,R-BICP)(DMF)<sub>n</sub>] (preparation given) in isopropanol, 5 mL isopropanol, and 125  $\mu$ L 0.1 M (12.5  $\mu$ mol) ethylenediamine in isopropanol. After stirring for several minutes, 73  $\mu$ L (625  $\mu$ mol) acetophenone was added, followed by 0.50 mL 0.1 M (50  $\mu$ mol) tetramethyl-2-tert-butylguanidine in isopropanol. The glass reaction vial containing the resulting mixture was sealed in an autoclave and then removed from the glovebox. The gas phase in the autoclave was replaced by hydrogen at 18 bar and the reaction mixture was stirred at room temperature for 6 h under 17-18 bar hydrogen to give, after silica gel chromatog., (S)-1-phenylethanol (77% e.e.).

L8 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:591066 HCAPLUS

DOCUMENT NUMBER: 139:151397

TITLE: Process for preparing nonracemic chiral alcohols by hydrogenation of ketones using ruthenium-based catalysts

INVENTOR(S): Tucker, Charles Edward; Jiang, Qiongzong

PATENT ASSIGNEE(S): Dsm N.V., Neth.

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061825	A1	20030731	WO 2002-NL826	20021213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003144521	A1	20030731	US 2002-57826	20020124
US 6743921	B2	20040601		
US 2003181318	A1	20030925	US 2002-158559	20020521
PRIORITY APPLN. INFO.:			US 2002-57826	A 20020124
			US 2002-158559	A 20020521
OTHER SOURCE(S):		MARPAT 139:151397		

AB The present invention provides a catalyst system and a process for the preparation of a nonracemic chiral alc. by hydrogenation of a ketone using the catalyst system, wherein the catalyst system comprises ruthenium, a nonracemic nonatropisomeric chiral diphosphine ligand, an achiral diamine ligand, and a base. Acetophenone was hydrogenated to S-1-phenethanol using a catalyst system containing RuCl<sub>2</sub>(benzene)<sub>2</sub>, (R,R,R,R)-2,2'-bis-(diphenylphosphino)-1,1'-dicyclopentane, 4,5-dimethyl-1,2-phenylenediamine, and sodium isopropoxide.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:405867 HCAPLUS

DOCUMENT NUMBER: 139:245838

TITLE: Chemoenzymatic synthesis of duloxetine and its enantiomer: lipase-catalyzed resolution of 3-hydroxy-3-(2-thienyl) propanenitrile

AUTHOR(S): Kamal, Ahmed; Khanna, G. B. Ramesh; Ramu, R.; Krishnaji, T.

CORPORATE SOURCE: Division of Organic Chemistry, Biotransformation Laboratory, Indian Institute of Chemical Technology, Hyderabad, 500 007, India

SOURCE: Tetrahedron Letters (2003), 44(25), 4783-4787  
CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:245838

AB An efficient and facile chemoenzymic synthesis of duloxetine by lipase-mediated resolution of 3-hydroxy-3-(2-thienyl)propanenitrile has been achieved. This process also describes an enantioconvergent synthesis of duloxetine via a Mitsunobu reaction.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:356091 HCAPLUS

DOCUMENT NUMBER: 138:353733

TITLE: Process for producing optically active amino alcohols

INVENTOR(S): Watanabe, Masahito; Murata, Kunihiro; Ikariya, Takao

PATENT ASSIGNEE(S): Kanto Kagaku Kabushiki Kaisha, Japan

SOURCE: Eur. Pat. Appl., 23 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1308435	A2	20030507	EP 2002-24517	20021030
EP 1308435	A3	20030604		
EP 1308435	B1	20051228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2003201269	A	20030718	JP 2002-251994	20020829
JP 3504254	B2	20040308		
CA 2409906	A1	20030430	CA 2002-2409906	20021028

JP 2003201270	A	20030718	JP 2002-316217	20021030
US 2003171592	A1	20030911	US 2002-285164	20021031
US 6686505	B2	20040203		

PRIORITY APPLN. INFO.:

JP 2001-335322	A	20011031
JP 2002-251994	A	20020829

OTHER SOURCE(S): MARPAT 138:353733

AB A process for producing an optically active amino alc. is provided that includes a step in which a nitro ketone or a cyano ketone is reacted with a hydrogen-donating organic or inorg. compound in the presence of a transition metal compound catalyst having an optically active nitrogen-containing compound as an asym. ligand to give an optically active nitro alc. or an optically active cyano alc., and a step in which the above optically active alc. is further reduced to efficiently produce an optically active amino alc. Thus, PhCOCH<sub>2</sub>CN was reduced with HCO<sub>2</sub>H in presence of Et<sub>3</sub>N and chloro[(S,S)-N-(p-toluenesulfonyl)-1,2-diphenylethylenediamine](p-cymene)ruthenium to give (S)-HOCHPhCH<sub>2</sub>CN in 98% ee. This compound was reduced with BH<sub>3</sub>.Me<sub>2</sub>S to give (S)-HOCHPhCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> with 98% ee. The alcs. are intermediates for pharmaceuticals, such as fluoxetine, tomoxetine, nisoxetine and norfluoxetine.

L8 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:173596 HCAPLUS

DOCUMENT NUMBER: 138:221463

TITLE: Process for preparation of  
3-(N-alkoxycarbonyl-N-methyl)amino-2-thienylpropan-1-ol derivatives

INVENTOR(S): Ikunaka, Masaya; Matsumoto, Jun; Inoue, Toru

PATENT ASSIGNEE(S): Nagase and Co., Ltd., Japan

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018572	A1	20030306	WO 2002-JP8588	20020826
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

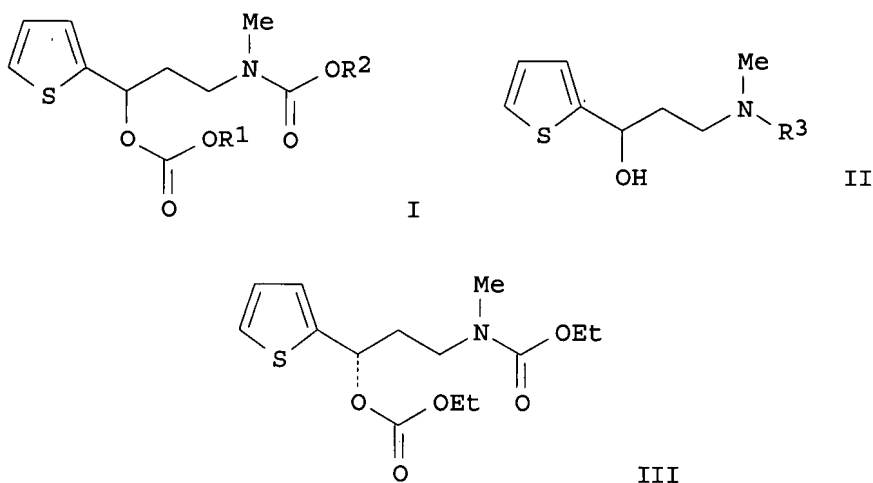
JP 2005053781 A 20050303 JP 2001-256621 20010827

PRIORITY APPLN. INFO.:

JP 2001-256621 A 20010827

OTHER SOURCE(S): MARPAT 138:221463

GI



AB This invention pertains to prepn method of novel optically active 3-amino-2-thienylpropan-1-ol derivs. with general formula of I and II [wherein R1 and R2 = independently (un)substituted alkyl, alkoxy, alkenyl, alkynyl, (hetero)aralkyl, or (hetero)aryl; R3 = H or CO2R2]. Reaction of optically active 3-(N,N-dimethylamino)-1-(2-thienyl)propan-1-ol with a haloformic ester in the presence of a base provides I. Hydrolysis of I affords alc. II. For example, (S)-3-(N,N-dimethylamino)-1-(2-thienyl)propan-1-ol (96.2% e.e.) was treated with Et chloroformate in PhMe in the presence of NaHCO<sub>3</sub> to give III (89%). Compound III was hydrolyzed with NaOH in EtOH and H<sub>2</sub>O to afford (S)-(2-thienyl)CH(OH)CH<sub>2</sub>CH<sub>2</sub>NHMe (80%) with 95.8% e.e.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL REGISTRY

COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
136.75	310.86

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
-19.50	-19.50

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FILE 'REGISTRY' ENTERED AT 07:29:10 ON 15 APR 2007

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 APR 2007 HIGHEST RN 930268-90-9

DICTIONARY FILE UPDATES: 13 APR 2007 HIGHEST RN 930268-90-9

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

10521799.trn

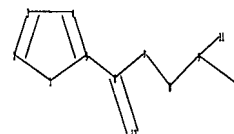
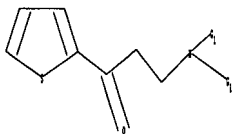
Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10521799a.str



chain nodes :  
6 7 8 9 11 12 13  
ring nodes :  
1 2 3 4 5  
chain bonds :  
5-6 6-7 6-12 7-8 8-9 9-11 9-13  
ring bonds :  
1-2 1-5 2-3 3-4 4-5  
exact/norm bonds :  
1-2 1-5 2-3 3-4 4-5 6-12 8-9 9-11 9-13  
exact bonds :  
5-6 6-7 7-8

G1:H,Ak

Match level :

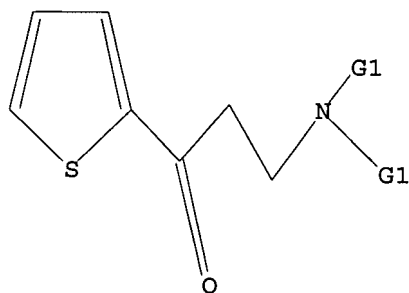
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS  
11:CLASS 12:CLASS 13:CLASS

L13 STRUCTURE UPLOADED

=> d 113

10521799.trn

L13 HAS NO ANSWERS  
L13 STR



G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l13

SAMPLE SEARCH INITIATED 07:29:29 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 242 TO ITERATE

100.0% PROCESSED 242 ITERATIONS 30 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 3907 TO 5773  
PROJECTED ANSWERS: 272 TO 928

L14 30 SEA SSS SAM L13

=> s l13 sss full

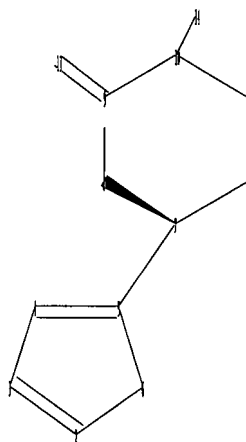
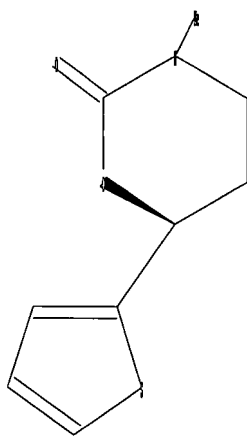
FULL SEARCH INITIATED 07:29:38 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 5232 TO ITERATE

100.0% PROCESSED 5232 ITERATIONS 494 ANSWERS  
SEARCH TIME: 00.00.01

L15 494 SEA SSS FUL L13

=>

Uploading C:\Program Files\Stnexp\Queries\10521799b.str



chain nodes :

13 14

ring nodes :

2 3 4 5 6 7 8 9 10 11 12

chain bonds :

5-7 9-13 10-14

ring bonds :

2-3 2-6 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12

exact/norm bonds :

7-8 7-12 8-9 9-10 9-13 10-11 11-12

exact bonds :

2-3 2-6 3-4 4-5 5-6 5-7 10-14

isolated ring systems :

containing 2 : 7 :

G1:H,Ak

Match level :

2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS 11:Atom  
12:Atom 13:CLASS 14:CLASS

Stereo Bonds:

8-7 (Single Wedge).

Stereo Chiral Centers:

7 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 7

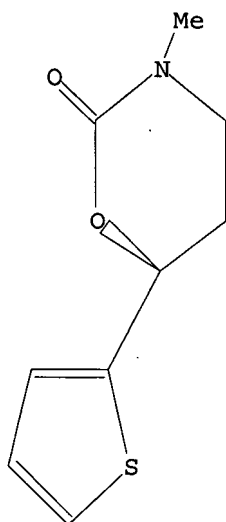
L16 STRUCTURE UPLOADED

=> d l16

L16 HAS NO ANSWERS

L16 STR





G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

=&gt; s l16

SAMPLE SEARCH INITIATED 07:34:36 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 2 TO 124

PROJECTED ANSWERS: 0 TO 0

L17 0 SEA SSS SAM L16

=&gt; s l16 sss full

FULL SEARCH INITIATED 07:34:45 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 37 TO ITERATE

100.0% PROCESSED 37 ITERATIONS

SEARCH TIME: 00.00.01

1 ANSWERS

L18 1 SEA SSS FUL L16

=&gt; FIL HCAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

347.35

658.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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-19.50

FILE 'HCAPLUS' ENTERED AT 07:34:50 ON 15 APR 2007

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FILE COVERS 1907 - 15 Apr 2007 VOL 146 ISS 17  
FILE LAST UPDATED: 13 Apr 2007 (20070413/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l18

L19

1 L18

=> d l19 ibib-abs hitstr tot

L19 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:101154 HCAPLUS

DOCUMENT NUMBER: 140:163699

TITLE: Process for the preparation of 3-hydroxy-(2-thienyl)propanamines by catalytic enantioselective hydrogenation of the corresponding ketones

INVENTOR(S): Hems, William; Rossen, Kai; Reichert, Dietmar; Koehler, Klaus; Almendra Perea, Juan Jose

PATENT ASSIGNEE(S): Degussa A.-G., Germany

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

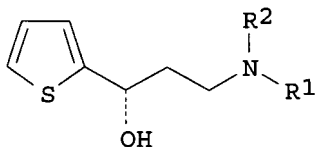
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

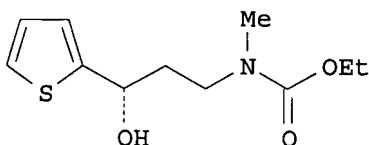
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011452	A1	20040205	WO 2003-EP7927	20030721
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10233724	A1	20040205	DE 2002-10233724	20020724
DE 10258098	A1	20040701	DE 2002-10258098	20021211
CA 2493228	A1	20040205	CA 2003-2493228	20030721

AU 2003258532	A1	20040216	AU 2003-258532	20030721
EP 1523479	A1	20050420	EP 2003-771063	20030721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1671685	A	20050921	CN 2003-817590	20030721
JP 2006502996	T	20060126	JP 2004-523756	20030721
US 2005272930	A1	20051208	US 2005-521799	20050121
IN 2005KN00259	A	20070105	IN 2005-KN259	20050224
PRIORITY APPLN. INFO.:			DE 2002-10233724	A 20020724
			DE 2002-10258098	A 20021211
			WO 2003-EP7927	W 20030721
OTHER SOURCE(S):			CASREACT 140:163699; MARPAT 140:163699	
GI				



I



II

AB Title compds. I [wherein R<sup>1</sup> and R<sup>2</sup> = independently H, (cyclo)alkyl, acyl, alkoxy carbonyl, (hetero)aryl, (hetero)aralkyl, alkylcycloalkyl, alkyl(hetero)aryl; or NR<sup>1</sup>R<sup>2</sup> = (un)substituted heterocyclyl], intermediates for the synthesis of enantiomer-pure bioactive substances, were prepared by catalytic enantioselective hydrogenation of the corresponding  $\alpha$ -heteroaryl ketones. Inter alia Ru catalysts with chiral diamine and chiral biphosphine ligands were used. For example, 3-[N-ethoxycarbonyl-N-methylamino]-1-(2-thienyl)-1-propanone was introduced to a Buchi stirred autoclave, which was then evacuated. A mixture of (R)-TolBINAP-RuCl<sub>2</sub>-(1R,2R)-diphenylethylenediamine and KOBu-t in iPrOH was added. Flushing with H<sub>2</sub>, pressurizing to 10 bar, and heating to 40° for 2 h provided II in >96% yield with an enantiomeric excess of 80.1%. The content of cyclic carbamate byproduct increased significantly after standing for a fairly long time.

IT 654062-24-5P, (S)-3-Methyl-6-(2-thienyl)tetrahydro-2H-1,3-oxazin-2-one

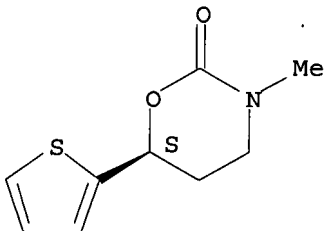
RL: BYP (Byproduct); IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(cyclic carbamate; preparation of 3-hydroxy-(2-thienyl)propanamines by catalytic enantioselective hydrogenation of corresponding ketones)

RN 654062-24-5 HCAPLUS

CN 2H-1,3-Oxazin-2-one, tetrahydro-3-methyl-6-(2-thienyl)-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10521799.trn

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

10.47

668.68

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-0.78

-20.28

STN INTERNATIONAL LOGOFF AT 07:35:46 ON 15 APR 2007